REMARKS

I. Status of the Claims

Claims 1-3, 6-11, 13-28 and 30 to 48 were pending for purposes of this Office Action, as claims 4, 5, 12 and 29 were previously cancelled. Claim 1 has been amended to indicate that the composition is a dry powder and comprises heparin and 2% or more w/w of leucine. Claim 6 has been amended to indicate that the composition further comprises a heparinoid. Claims 22 and 23 have been amended to clarify that MMAD refers to "mass median aerodynamic diameter". Claims 47 and 48 have been amended to conform with the change in claim 1 of amino acid to leucine. Claims 2, 3, 6-11, 13-25 and 41-48 have been amended to properly depend them from a method claim, rather than a composition. Claim 43 has been corrected to refer to "fine particle fraction" instead of "fine particle dose". New claims 49 and 50 have been added. Claims 9 and 26-28 have been cancelled, without prejudice.

Support for the amendments and new claims can be found throughout the specification and specifically in Tables 2 and 3 of the specification as filed. Claims 1-3, 6-8, 10-11, 13-25 and 30 to 50 remain pending.

Applicant respectfully submits that no new matter has been added by virtue of this amendment.

Reconsideration is respectfully requested.

II. Claim Rejections- 35 U.S.C. § 112

Claims 22 and 23:

In the current Office Action, Claims 22 and 23 were rejected under 35 U.S.C. § 112, second paragraph, because they recited the abbreviation MMAD without defining what the abbreviation stands for. In response, the abbreviation MMAD has been removed

from Claims 22 and 23 and replaced with the phrase "mass median aerodynamic diameter".

Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

III. Claim Rejections- 35 U.S.C. § 103

Claims 1-3, 6-10, 14-28, 30, 40-42 and 44-48

In the current Office Action, claims 1-3, 6-10, 14-28, 30, 40-42 and 44-48 were rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649).

Claims 9 and 26-28 have been cancelled by way of the present amendment. Therefore, the rejection to these claims is now moot.

The Ahmed et al. reference discloses heparin and ultra low molecular weight heparin (ULMWH) or other sulfated polysaccharides having average molecular weights of about 1,000-3,000 daltons for the treatment of late phase allergic reactions, airway hyperresponsiveness or inflammatory reactions/diseases. See Ahmed, abstract. The Ahmed et al. reference also teaches that ULMWH may be administered by inhalation and provides methods and formulations for aerosol delivery.

The Staniforth reference describes a powder for use in a dry powder inhaler comprising active material and additive material; the additive material comprising an anti-adherent material and the powder includes at least 60% by weight of active materials. See Staniforth, Abstract.

Claim 1 of the present invention as currently amended recites: A method of treating a pulmonary disease comprising the administration of a therapeutically effective

amount of a pharmaceutical composition to a subject in need of such treatment, wherein the pulmonary disease has as a symptom the excess formation of mucus secretions in the airways, said pulmonary disease is selected from the group consisting of chronic bronchitis, acute asthma, cystic fibrosis, chronic obstructive pulmonary disease and bronchiectasis, said composition comprising one or more mucoactive agents which assist mucous clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus, and digesting naked DNA and cell debris within the mucus, wherein the composition is a dry powder **and comprises heparin and 2% or more w/w of leucine.** (emphasis added)

As seen above, Claim 1 has been amended to recite that the composition "comprises heparin and 2% or more w/w of leucine". On pages 7-8 of the October 28, 2008 Office Action, the Examiner acknowledged that the "results indicated by Applicant only concern a single synergistic combination, heparin and leucine". The Examiner then argued that the results shown by Applicants did not demonstrate results for either the full scope of glycosaminoglycans or the full scope of amino acids. As Claim 1 now recites the combination of heparin and 2% or more w/w of leucine, Applicants respectfully submit that the Examiner's objections have been overcome.

In furtherance of the above, Applicants respectfully remind the Examiner that the Ahmed reference does not teach the inclusion of amino acids in a heparin formulation. As such, it cannot teach or suggest the combination of heparin and 2% or more w/w of leucine as recited in claim 1 of the present invention, nor does it provide a reason for a person of ordinary skill in the art to adapt or modify the heparin composition disclosed therein by combining heparin with 2% or more of leucine.

The Staniforth reference cited in the Office Action does not cure this deficiency of the Ahmed et al. reference. The Staniforth reference at page 13, lines 22-30 and in Example 8 teaches that the addition of large amounts of additive material (e.g. leucine) does not improve the properties of the resulting powder and can have a detrimental impact on the respirable fraction. Further, the Staniforth reference not only indicates that the addition of 5% or 10% by weight of

leucine does not give better results than 1% leucine, it also indicates that the increased amount of leucine actually results in a decrease in the respirable fraction. See the Staniforth Reference at page 13, lines 22-30 and Example 8.

In contrast, as seen from Tables 2 and 3 of the present invention, Applicants have unexpectedly discovered that for the combination of heparin and 2% or more of leucine, the respirable fraction significantly increases as the percentage of leucine is increased.

On page 7 of the Office Action, the Examiner cites Example 3 of the Staniforth reference to provide support for the Staniforth reference teaching a composition containing 2% of leucine as a usable embodiment of the Staniforth invention. However, Example 3 teaches the combination of leucine powder with terbutaline sulphate powder, not heparin. As explained on page 13, line 13-16, the ratio in which the additive material and the active material are present in the powder will depend on the type of inhaler device used, the type of active material used and the required dose. The Staniforth reference further clarifies on page 13, line 34-36 that "[t]he optimum amount of additive will depend of the active material and additive material used. Terbutaline is a beta adrenergic agonist. Heparin is a member of the glycosaminoglycan family of carbohydrates. As such, the combination of terbutaline suphate and 2% of leucine cannot teach the unexpected results achieved in the present invention through the combination of heparin and 2% or more w/w of leucine.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al. reference and the Staniforth reference does not render claim 1 of the present invention obvious. Claims 2-3, 6-8, 10, 14-25, 30, 40-42, and 44-48 either directly or indirectly depend from claim 1 these claims also are not rendered obvious in view of combination of the Ahmed et al. reference and the Staniforth reference.

Applicant points out that new claim 49 recites: A composition for assisting mucus clearance, the composition **comprising heparin and 2% or more w/w of leucine**, wherein the composition is dry powder for pulmonary inhalation and assists mucus clearance through one or more of the following mechanisms: reducing cross-linking within the mucus, diluting the mucus;

and/or digesting naked DNA and cell debris within the mucus. For the same reasons as discussed above for claim 1, claim 49 which also recites a composition **comprising heparin and 2% or more w/w of leucine**, is not rendered obvious by the combination of the Ahmed et al. and Staniforth references.

Applicant therefore requests withdrawal of the rejections to claims 1-3, 6-8, 10, 14-25, 30, 40-42, and 44-48 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) and further in view of Staniforth (PCT International Publication WO97/03649).

Claims 31-34

In the Office Action, claims 31-34 were rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6-10, 14-30, 40-42 and 44-48, and further in view of Dunbar et al.

Claim 1 as amended, recites in pertinent part "wherein the composition ... comprises **heparin and 2% or more w/w of leucine**". (emphasis added) The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claims 31 to 34 depend indirectly from claim 1.

The Dunbar reference relates to the evaluation of a plain-jet atomizer and ultrasound nebulizer for use in a spray drying tower for the production of respirable dry particles. See Dunbar, page 440, first paragraph under "Conclusion" heading. Thus, Dunbar concerns the analysis of the production of spray-dried particles.

The Dunbar reference does not teach or suggest a method of treating a pulmonary disease comprising administering a composition comprising heparin and 2% or more w/w of leucine. Therefore the Dunbar reference does not cure the defect of either the Ahmed reference or the

Staniforth reference.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al., Staniforth and Dunbar references does not render claims 31 to 34 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claims 31 to 34 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. in view of Staniforth, and further in view of Dunbar et al.

Claims 11 and 35-39

In the current Office Action, claims 11 and 35-39 were rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6-10,14-30, 40-42 and 44-48 above, and further in view of Chickering et al. (US2004/0121003).

Claim 1 as amended, recites in pertinent part "wherein the composition ... comprises **heparin and 2% or more w/w of leucine**". (emphasis added) The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claims 11 and 35 depend directly from claim 1 and claims 36-39 depend indirectly from claim 1.

The Chickering et al. reference relates to a method for making a dry powder blend comprising jet milling particles of a pharmaceutical formulation to deagglomerate at least a portion of the microparticles which may have agglomerated while substantially maintaining the size and morphology of the individual microparticles. See Chickering et al., abstract.

The Chickering reference does not teach or suggest a method of treating a pulmonary disease comprising administering a composition comprising heparin and 2% or more w/w of leucine. Therefore, the Chickering reference does not cure the defect of either the Ahmed reference or the Staniforth reference.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al., Staniforth and Chickering references does not render claims 11 and 35-39 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claims 11 and 35-39 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. in view of Staniforth, and further in view of Chickering et al.

Claim 13

In the current Office Action, claim 13 was rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 1-3, 6-10, 14-30, 40-42 and 44-48 above, and further in view of Stossel et al. (U.S. Patent 5,464,817).

Claim 1 as amended, recites in pertinent part "wherein the composition ... comprises **heparin and 2% or more w/w of leucine**". (emphasis added) The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claim 13 depends directly from claim 1.

The Stossel reference is directed to methods of promoting respiratory tract flow by administering actin-binding proteins. See Stossel, col. 1, lines 18 to 26.

The Stossel reference does not teach or suggest a method of treating a pulmonary disease comprising administering a composition comprising heparin and 2% or more w/w of leucine. Therefore, the Stossel reference does not cure the defect of either the Ahmed reference or the Staniforth reference.

For the foregoing reasons, Applicants submit that the combination of the Ahmed et al. reference, Staniforth reference and Stossel et al. reference does not render claim 13 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the

rejections to claim 13 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al., in view of Staniforth and further in view of Stossel et al.

Claim 11

In the current Office Action, claim 11 was rejected under 35 U.S.C. § 103(a) as being obvious over Ahmed et al. (PCT International Publication No. WO99/06025) in view of Staniforth (PCT International Publication WO97/03649) as applied to claims 3, 6-10,14-30, 40-42 and 44-48 above, and further in view of Trofast et al. (U.S. Patent 6,027,714).

Claim 1 as amended, recites in pertinent part "wherein the composition ... comprises **heparin and 2% or more w/w of leucine**". (emphasis added) The Ahmed et al. reference and the Staniforth reference are discussed above with respect to claim 1. Claim 11 depends directly from claim 1.

The Trofast reference describes a dry powder composition comprising budesonide and a carrier substance for use as a treatment of respiratory disorders. See Trofast, col. 1, lines 23 to 27.

The Trofast reference does not teach or suggest a method of treating a pulmonary disease comprising administering a composition comprising heparin and 2% or more w/w of leucine. Therefore, the Trofast reference does not cure the defect of either the Ahmed reference or the Staniforth reference.

For the foregoing reasons, Applicants submit that the combination of Ahmed et al., Staniforth et al., and the Trofast et al. references does not render claim 11 of the present invention obvious. In view of the foregoing, Applicant respectfully requests withdrawal of the rejections to claim 11 under 35 U.S.C. § 103(a) as being obvious over Ahmed et al., in view of Staniforth, and further in view of Trofast et al.

CONCLUSION

Reconsideration of the present application, as amended, is requested. The Examiner is respectfully requested to telephone Applicant's undersigned attorney in order to resolve any outstanding issues and advance the prosecution of the case to allowance.

This response is being submitted together with a petition for three-month extension of time and the fee due under 37 C.F.R. § 1.17(a)(3). By virtue of this Response, Applicants have added one new independent claim and one new dependent claim. According to Applicants' calculation no fee is due for these new claims. If it is determined that additional fees are due, the Commissioner for Patents is hereby authorized to charge said fees to Attorney Deposit Account 50-0552.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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